REMARKS

The Official Action of December 16, 2003 has been carefully considered and reconsideration of the application as amended is respectfully requested.

Applicants note that the Examiner has made the requirement for restriction final and has refused to examine claims 21 and 23 or Group XIV in the present application. Applicants respectfully request reconsideration of this decision. As set forth in Annex B of the Administrative Instructions Under the PCT, the method for determining unity of invention under PCT Rule 13 shall be construed as permitting, in claims of different categories:

> "in addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for a use of the said product"

In the present case, this would mandate inclusion of an independent claim to isolated nucleotide (claim 2) and an independent claim to the use thereof (claim 37).

The Examiner has considered the question of unity with respect to claim 1 only, but this is respectfully not a proper analysis. PCT Rule 13 requires that unity has to be considered in relation to the independent claims in an application, not just to the first claim. Moreover, the Examiner's contention that the elected invention does not make a contribution over the prior art is respectfully believed to be incorrect as discussed below.

Claim 1 has been amended in accordance with the disclosure at, for example, page 24, lines 15-19, and page 25, lines 11-17, to reflect that the claimed nucleic acid is from a hepatitis B virus strain glycine 145 arginine of subtype *adw*. By virtue of this amendment, the claims more clearly distinguish over the cited art (see discussion below). Claim 9 has been amended to remove the basis for the rejection under 35 USC 112, second paragraph appearing on page 3 of the Official Action.

Claim 4 is objected under 37 CFR 1.75(c) as being of improper dependent form for allegedly failing further to limit the subject matter of claim 3. However, although claim 3 requires that the recited polypeptide comprise nucleotides 155 through 835 of SEQ ID NO: 3, it does not require that the nucleotides be in designated positions within the polypeptide. Thus, the recited polypeptide can also contain other nucleotides and need not have "AGA" at positions 587-589. Accordingly, claim 4 does further limit claim 3 and it is respectfully submitted that the objection should be withdrawn.

Certain claims stand rejected under 35 USC 102(b) as allegedly being anticipated by WO 91/14703. Certain claims stand rejected under 35 USC 102(b) as allegedly being anticipated by Oon et al. Other claims stand rejected under 35 USC 103 as allegedly being unpatentable over Oon et al in view of WO 91/14703. Applicants respectfully traverse these rejections.

The claims as amended define an isolated nucleic acid of a new hepatitis B

Virus Strain Glycine 145 Arginine of subtype *adw*. Research on these strains show that this subtype is common in the Asian Pacific region, and has the following distinguishing characteristics:

(a) subtype *adw* is poorly antigenic (Chen W.C., Oon C.J., Toh I. Altered antigenicities of hepatitis B surface antigen carrying mutation outside the common 'a' determinant. Journal: American Journal of Gastroenterology, Vol 95, No: 4, 2000).

(b) Associated with hepatocellular Carcinoma (C.J. Oon, W.N. Chen Zhao Y, Feng S.A., Leong A.I.) "Detection of human hepatiis B surface mutants and their integration in human hepatocellular Carcinoma.

(c) Transmissible intrafamily, even in the presence of antiHBs and that there are several different strains of glycine 145 arginine within the *adw* subtype family. (Journal of Infection (2000) 4. 260-264, C.J. Oon, Chen W.N., Goo K.S., Goh ICT. "Intrafamilial Evidence of Horizontal transmission of Hepatitis B Virus Surface antigen mutant G145R.")

By contrast, the WO 91/14703 reference refers to a different subtype (subtype *ayr*), which cannot be expected or assumed to comprise the same nucleotide sequences. Indeed, the strain described in the reference is Mediterranean and has not even been shown to have the same function and disease causation as the claimed strains. Accordingly, it is respectfully submitted that the Examiner cannot rely on this reference to set forth even a *prima facie* case of novelty or nonobviousness.

Similarly, the Oon et al reference does not disclose the *adw* subtype. Indeed, prior to the filing of the present application, there has been no publication by the present inventors or others of the detailed molecular structure and sequence of the whole G145R strain *adw*. This information has also not been published in the Gene bank. This being the case, and since a reference cannot be anticipatory if it does not contain an enabling disclosure of the allegedly anticipatory subject matter, the Examiner also cannot rely on this reference to set forth even a *prima facie* case of novelty or nonobviousness.

In view of the above, it is respectfully submitted that all rejections and objections of record have been successfully traversed and that the application is now in allowable form. An early notice of allowance is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,

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